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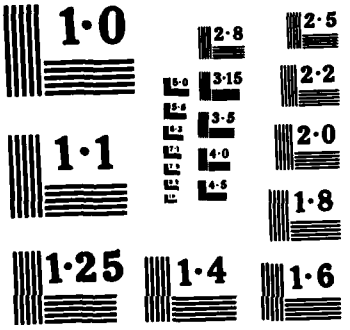

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AD-A157 694

PULMONARY ADAPTATION TO HIGH ALTITUDE

SEMI-ANNUAL PROGRESS REPORT - YEAR 08
(Dec. 1984 - June 1985)

Jerome A. Dempsey, Ph.D.

June 1985

Supported by

U.S. ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND
Fort Detrick, Frederick, MD 21701

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Annual Progress Report

(Year 08 - Nov. 05, 1984 to June 1, 1985)

[First half of final year of a 2-year contract,

Dec. 1, 1983 to Nov. 30, 1985]

Three major aims of the contract were addressed in the past 6 months:

1. We completed our study of the relationship between hypoxia-induced periodic breathing in sleep and the occurrence of obstructive apnea. We used normal subjects and those who might be "susceptible" to upper airway closure, i.e., heavy snorers and even some patients with obstructive sleep apnea syndrome. As expected we found that administration of hypoxia caused immediate hypocapnia leading to a Cheyne-Stokes type of oscillatory breathing pattern which caused marked increases in airway resistance during the periods of low ventilatory drive. The surprising finding was that once full-blown periodic breathing developed--after about 5 mins of hypoxia--airway resistance was markedly reduced to levels $\bar{<}$ than those observed while awake and no evidence of occlusive apnea occurred. The conclusion is that hypoxia must have exerted a protective effect on the upper airway, by ensuring that as inspiratory drive increased toward the end of each apneic period, activity to the muscles controlling upper airway caliber was greater than and/or preceded that to the diaphragm and other inspiratory muscles of the chest wall. Further studies are now needed of the EMG activity of these upper airway and chest wall muscles to determine their relative activities during the apneic periods. This "protective" mechanism is central to the sojourner at high altitude--particularly the

heavy snorer--to guard against occlusive apnea and even greater nocturnal hypoxemia. (This work was presented at the recent American Thoracic Society Meeting.

2. The question of respiratory muscle fatigue during exercise in humans was studied in highly fit subjects performing high intensity exercise to exhaustion. First we found that a partial "unloading" of ventilatory work--by breathing low density He:O_2 gas mixtures--significantly increased exercise endurance time to exhaustion and reduced "perception" of effort. On the other hand our additional data did not implicate the mechanical work of breathing during exhaustive exercise as an inportant contribution to overall fatigue. We determined the pleural pressure wave form and magnitude generated each breath during exhaustive exercise. Then we mimicked this form and magnitude of pressure development at rest and found that the subject could tolerate this form of pressure development for much longer times than he could exercise. Work coninues on this project in normoxic and hypoxic conditions. (Aaron et al., Med. Sci. Sport, 1985 (Abstract).

3. We have studied respiratory muscle recruitment during exercise and saw evidence of active expiration even in mild exercise. We documented this by measuring the change in FRC and in end-expiratory value and in esophageal and gastric pressures. We have also documented this change by recording abdominal muscle EMG activity even at light work loads. (see Sharatt, Med. Sci. Sport, 1985 Abstract) and Henke, Med. Sci Sport, 1985 Abstract).

4. Finally, we have presented the concept in two recent reviews and presentations (Am. J. Cardiology, 1985; and Wolffe Memorial Lecture, American College of Sports Medicine, May 1985) that the lung becomes a

"limiting" factor to exercise capacity as one proceeds from an untrained state to a highly trained state, because training causes adaptation of the locomotor muscles but not the respiratory muscles nor the lung. Eventually the capability for O_2 uptake by the locomotor muscles becomes greater than that afforded by the O_2 transport capabilities of the lung and chest wall. This selective effect of physical training contrasts markedly with that of the long-term resident of high altitude who shows true structural adaptation of the pulmonary system.

Publications supported all or in part by Contract No. DAMD 17-82-C-2259.
Contract Year 07 & 08 (November 1983 - June 1985).

Manuscripts Published or in Press

1. Bersenbrugge, A., J. Dempsey, C. Iber, J. Skatrud, and P. Wilson. Mechanisms of hypoxia-induced periodic breathing during sleep in humans. J. Physiol. (London) 343:507-524, 1983.

2. Berssenbrugge, A., J. Dempsey, and J. Skatrud. Hypoxic Versus Hypocapnic Effects on Periodic Breathing During Sleep. In: High Altitude and Man, American Physiological Society, 115-127, 1984.

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4. Dempsey, J.A. Ventilatory control during sleep in hypoxia: Overview. Hypoxia Symposium III, Banff, Canada, January 1983 (J. Sutton and C. Houston, editors). Progress in Clinical and Biological Research, Vol. 136:61-64, 1984.

5. Dempsey, J., J. Skatrud and A. Berssenbrugge. Sleep in hypoxia. In: Contemporary Issues in Pulmonary Disease, editors N. Edelman and N. Cherniack (in press).

6. Dempsey, J.A., E.H. Vidruk, and G.S. Mitchell. Regulation of pulmonary control systems during exercise: update. Fed. Proc. 44:2260-2270, 1985.

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8. Fregosi, R. and J. Dempsey. Regulation of arterial acid-base status in the exercising rat. J. Appl. Physiol. 57:396-402, 1984.

9. Dempsey, J., and R. Fregosi. Adaptability of the pulmonary system to increased metabolic demand. Am. J. Cardiology 55:(10):59D, April 1985.

10. Hussain, S.N.A., R.L. Pardy and J. Dempsey. Mechanical impedance as a determinant of inspiratory neural drive during exercise in healthy humans. (In Press, J. Appl. Physiol.).

11. Skatrud, J.B. and J.A. Dempsey. Sleep effects on pulmonary mechanics in snorers and non-snorers. J. Appl. Physiol. (in press).

12. Wilson, P., J.B. Skatrud, and J.A. Dempsey. Effects of slow-wave sleep on ventilatory compensation to inspiratory elastic loading in humans. Respir. Physiol. 55:103-120, 1984.

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1. Hussain, S.N.A, R.L. Pardy and J. Dempsey. "Pulmonary impedance as a determinant of inspiratory neural drive during exercise." Fed. Proc. 43:1412, 1984.

2. Fregosi, R., H.S. Hoff and J.A. Dempsey. "Effects of short-term exercise on locomotor and diaphragm muscle metabolism." Fed. Proc. 43:3590, 1984.

3. Smith, C., et al. "Carotid bodies are required for ventilatory acclimatization to moderate and severe hypoxia." Physiologist 27:13-4, 1984.

4. Sharratt, M.T., K.G. Henke, D.F. Pegelow, E. Aaron, and J. Dempsey. "Exercise induced changes in functional residual capacity (FRC)." Medicine and Science in Sports and Exercise 17(2):290, 1985.

5. Aaron, E.A., K.G. Henke, D.F. Pegelow and J.A. Dempsey. "Effects of mechanical unloading of the respiratory system on exercise and respiratory muscle endurance." Medicine and Science in Sports and Exercise 17(2):290, 1985.

6. Henke, K.G., M.T. Sharratt, D.F. Pegelow, E. Aaron, and J. Dempsey. "Contributions of active expiration to inspiration during exercise." Medicine and Science in Sports and Exercise 17(2):289, 1985.

7. Begle, R., J. Skatrud, and J. Dempsey. "Ventilatory compensation for change in diaphragmatic length during sleep." Am. Rev. Resp. Disease, April 1985.

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9. Fregosi, R., M. Sanguq, D. Paulson, and J.A. Dempsey. "Diaphragm, plantaris and whole animal bioenergetics with endurance training." Medicine and Science in Sports and Exercise 17(2):257, 1985.

10. Warner, G., J. Skatrud, and J.A. Dempsey. "Effect of hypoxic-induced periodic breathing during sleep on upper airway obstruction." Am. Thoracic Society poster session, May 12-15, 1985

Military Significance

Our contract work is aimed at a better understanding of two physiological problems occurring in hypoxic environments which clearly affect the well-being and performance capabilities of the human sojourner at high altitudes. These problems are periodic breathing during sleep leading to loss of quality sleep and the resulting daytime hypersomnalence and fatigue; and the regulation of the ventilatory response and pulmonary gas exchange during exercise in hypoxia which are key determinants of exercise performance.

Our work on periodic breathing during hypoxic sleep provides the first comprehensive, quantitative description of this problem and provides the first definitive evidence detailing the major causes of periodicity and the reasons behind the beneficial effects of acute O_2 administration. Further, our more recent data suggests that acclimatization over a matter of a few days at high altitude may greatly alleviate periodic breathing during sleep. However, this remains a highly individual characteristic which we were unable to predict from available measurements. Indeed, the test of acute hypoxic ventilatory response--which is commonly used as a predictor of many facets of acclimatization--had no predictive value at all for the occurrence or severity of periodic breathing in hypoxic sleep.

Exercise capacity as determined by the pulmonary system in hypoxia and the debilitating symptoms of dyspnea which accompany exercise in hypoxia have been the subject of our investigations. Our work has detailed the critical limitations to oxygen transport presented by the failure of the lung's gas exchange and ventilatory control system and chest wall mechanics to respond adequately and/or efficiently to heavy work in hypoxic environments. Further, the baseline work in normoxic environments clearly shows the susceptibility of some highly fit individuals to these problems during exercise, thereby providing a basis for prediction of problems with high altitude exercise from measurements made at sea-level. We also showed the simple use of exercise tests in acute hypoxia--even using non-invasive measurements of arterial O_2 saturation--should provide excellent prediction of gas exchange "failure" at high altitudes. Our recent findings also strongly implicate a highly significant role for pulmonary and chest wall mechanics in the regulation of ventilation--and thus of gas exchange--during exercise--especially hypoxic exercise. We would predict with some confidence that the sea-level native with even "mild," asymptomatic airway disease (such as that due to chronic cigarette smoking or the mostly reversible airway disease of the otherwise healthy asthmatic) will have substantial problems in maintaining arterial oxygenation and/or avoiding extreme dyspnea during exercise at even mild elevations in altitude.

Facilities and Personnel

No changes were made in the past year.

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